Hepatitis C

Overview

Hepatitis C Disease Overview[i]

The Hepatitis C Virus ("HCV")

- Seven known genotypes (1 – 7), greater than 67 subtypes (1a, 1b, etc)
    - Treatment guidelines address genotypes 1 - 6
- Genotype 1b often results in the most aggressive form of liver disease and is resistant to interferon ("PEG") therapy
- Genotype 1a viruses may have a NS3 Q80K polymorphism (see below)

Acute and Chronic Disease

- Acute Hepatitis C
    - Often asymptomatic
    - Mean incubation of 50 days; virus can be detected in blood 3 weeks from infection date
    - Coinfection with Human Immunodeficiency Virus ("HIV") and/or a history of chronic alcohol use can increase the severity of acute hepatitis C
    - Acute hepatitis C may be resolved or may evolve into chronic hepatitis C
- Chronic Hepatitis C
    - Often asymptomatic until cirrhosis, end-stage liver disease and/or hepatocellular carcinoma develop, which can take years or even decades
    - Liver biopsy, not severity of symptoms or serum transaminase levels, is the best indicator of disease severity

Treatment Goals and Approaches[i]

Acute and Chronic Hepatitis C Treatment Goals

- Increase quality of life
- Decrease acute morbidity and mortality
- Minimize the spread of infection
- Stop hepatic inflammation (normalize aminotransferases)
- Prevent end-stage liver disease
- Stop viral replication in the patient
- Eradicate the virus = cure!

Treatment Approaches

- Acute Hepatitis C
    - Supportive (symptomatic) care - may require hospitalization for severe symptoms
    - Acute hepatitis C may be resolved or may evolve into chronic hepatitis C
- Chronic Hepatitis C
    - Regular monitoring of qualitative and quantitative measures
    - Determination of disease progression
    - Pharmacologic treatment - Timing of initiation should be discussed in depth with the patient
        - It may <u>not</u> be best to immediately start treatment if the disease is in its early stages
        - Adverse drug effects must be considered

        - Improved efficacy and reduced side effects of new and soon-to-be-released drugs may warrant waiting unless the patient needs immediate treatment
    - Liver support systems (liver dialysis)
    - Liver transplant

Acronyms & Definitions[i,ii]

Acronyms

- HIV = human immunodeficiency virus
- NS3 Q80K polymorphism = a particular type of Hepatitis C genotype 1a. It does not respond well to, and should not be treated with simeprevir
- PEG = pegylated interferon, a drug used to treat hepatitis C. "PEG" and "interferon" are sometimes used interchangeably
- RIBA = ribavirin, a drug used to treat hepatitis C
- RNA = ribonucleic acid = large molecules possessed by both viruses and humans that regulate genes. Viral RNA uses the human body's normal processes to replicate and spread infection.
- SVRx = Sustained Virologic Response = a laboratory value indicating the absence of detectable hepatitis C virus in blood x weeks after discontinuing treatment (e.g. SVR12 at 12 weeks, SVR24 at 24 weeks, etc.) The current regulatory standard is SVR12. If "SVR" (with no number) is referenced, assume SVR12.
- Viral Load = the amount of detectable hepatitis C virus in the blood

Patient Treatment History

- Treatment-naïve = no previous Hepatitis C treatment
- Response = Hepatitis C virus is undetectable in blood and liver function tests are normal immediately after treatment and sustained for 6 months
- Nonresponse = Failure = Hepatitis C virus is detectable and/or liver function tests are abnormal as therapy progresses. Therapy is usually stopped
- Relapse = Hepatitis C virus is undetectable and liver function tests are normal immediately after treatment, but re-emerge in the 6 months following therapy
- Interferon-ineligible (PEG-ineligible) = patient is not a candidate for treatment with PEG-interferon for one or more of a variety of reasons (autoimmune disorders, decompensated hepatic disease, etc.)

Pharmacotherapy for Hepatitis C[ii,iii,iv,v,vi]

- PEG (various brand names) = pegylated interferon, injected subcutaneously once weekly. Interferons decrease cell growth and increase cell death via a variety of mechanisms. Pegylated interferon is interferon to which inert polyethylene glycol has been chemically bound. Pegylated interferon remains in the body longer than non-pegylated interferon, and thus can be administered less often than non-pegylated interferon. "PEG" and "interferon" are sometimes used interchangeably.

- RIBA (various brand names, also available generic) = ribavirin, an oral capsule or solution taken twice daily. Ribavirin is a nucleoside which inhibits viral replication by stopping initiation and elongation of viral RNA fragments via a variety of mechanisms.
- Boceprevir (Victrelis®) = an oral capsule taken three times daily. Boceprevir is a first generation protease inhibitor targeted to a specific protease. It inhibits viral replication and is considered a direct-acting antiviral treatment for hepatitis C. Boceprevir became available in 2011.
- Simeprevir (Olysio®) = an oral capsule taken once daily. Simeprevir is a protease inhibitor targeted to a specific protease. It inhibits viral replication and is considered a direct-acting antiviral treatment for hepatitis C. It has low efficacy against, and should not be used to treat Hepatitis C genotype 1a with the NS3 Q80K polymorphism. Simeprevir became available in January (2014).
- Sofosbuvir (Sovaldi®) = an oral tablet taken once daily. Sofosbuvir is a polymerase inhibitor. It inhibits a specific polymerase and is considered a direct-acting antiviral treatment for hepatitis C. Sofosbuvir became available in January (2014).
- Telaprevir (Incivek®) = an oral tablet taken twice daily. Telaprevir inhibits viral replication. Telaprevir is a first generation protease inhibitor targeted to a specific protease. It inhibits viral replication and is considered a direct-acting antiviral treatment for hepatitis C. Telaprevir became available in 2011.

Drugs Currently Available to Treat Hepatitis C

Interferon	Nucleoside	First Generation Protease Inhibitor	Second Generation Protease Inhibitor	Polymerase Inhibitor
PEG	RIBA	Boceprevir (2011, Victrelis®) Telaprevir (2011, Incivek®)	Simeprevir (2014, Olysio®)	Sofosbuvir (2014, Sovaldi®)

The Evolution of Hepatitis C Standard of Care[ii,vii,viii,ix,x]

- 2009 AASLD Guidelines
  - Only PEG and RIBA were available

2009 Guidelines and Virologic Response Rates			
Genotype	Treatment	Duration	SVR
1	PEG + RIBA	48 weeks	~ 50%
2 and 3	PEG + RIBA	24 weeks	~ 80%

- 2011 AASLD Guidelines
  - PEG, RIBA, and first generation protease inhibitors were available (boceprevir, 2011 and telaprevir, 2011)

2011 Guidelines and Virologic Response Rates			
Genotype	Treatment	Duration	SVR
1	PEG + RIBA + First Generation Protease Inhibitor	24 to 48 weeks	~ 60 - 79%
2 and 3	PEG + RIBA	24 weeks	~ 80%

- 2014 AASLD / IDSA Guidelines
  - PEG, RIBA, boceprevir 2011, simeprevir 2014, sofosbuvir 2014 and telaprevir 2011 are available

2014 Guidelines and Virologic Response Rates			
Genotype	Treatment	Duration	SVR
See attached document			≤ ~ 97%

Pause for

Public Comment

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Resume DUR Discussion:

Treatment Costs

Hepatitis C Treatment Costs to Medicaid[ii,xi]

- Drug Costs

Hepatitis C Treatment Costs to Medicaid			
Drug	Least Costly Complete Course of Therapy	Most Costly Complete Course of Therapy	Maximum Percentage of Patients Achieving SVR
Boceprevir (2011, Victrelis®)	$7,069.02	$11,680.03	75% [xii,xiii]
Simeprevir (2014, Olysio®)	$51,254.72	$114,246.32	95% [xiv,xv,xvi]
Sofosbuvir (2014, Sovaldi®)	$63,915.60	$127,831.20	100% [xvii,xviii]
Telaprevir (2011, Incivek®)	$32,856.11	$34,242.11	88% [xix,xx,xxi]

- Tolerability for Patients (Quality of Living Costs)
  - Older drugs
    - Boceprevir 2011 = Anemia, neutropenia, dysgeusia, must take with food, many drug-drug interactions, must take many capsules daily
    - Telaprevir 2011 = Rash, anemia, anorectal symptoms, must take with fatty food, many drug-drug interactions, must take many tablets daily
  - Newer drugs
    - Simeprevir 2014 = Rash, photosensitivity, increased bilirubin, must take with food, fewer drug-drug interactions, PEG-free treatment options, once-daily dosing. Should not be used to treat Hepatitis C genotype 1a with the NS3 Q80K polymorphism
    - Sofosbuvir 2014 = Fatigue, headache, nausea, insomnia, may take without regard to food, fewer drug-drug interactions, PEG-free treatment options, once-daily dosing, pangenotypic
- Health Care Costs
  - The economic burden of a patient with hepatitis C is estimated to be substantially greater than that of a patient without hepatitis C. Various studies have estimated the cost differences of one patient with hepatitis C per year versus one patient without hepatitis C per year, including inpatient stays
    - Before simeprevir and sofosbuvir (pre-2014): $3,200 [xxii] to $15,500 [xxiii]
      - A patient that is "cured" will recover the drug costs in two to eleven years
    - After simeprevir and sofosbuvir: Too early for any studies, but using the figures above…
      - A patient that is "cured" will recover the drug costs in three to forty years

Other Payers' Policies

- Medicaid Accountable Care Organizations (ACOs)
    - Boceprevir 2011
        - All require prior authorization
    - Simeprevir 2014
        - Not yet reviewed
    - Sofosbuvir 2014
        - Not yet reviewed
    - Telaprevir 2011
        - All require prior authorization

Possible Prior Authorization Criteria for Hepatitis C Treatments

- Note: The Board discussed boceprevir and telaprevir in 2011, shortly after they came to market. It was decided that no prior authorization should be required.
    - They offed significantly better outcomes than PEG + RIBA therapy, the previous standard of care
    - Chances for abuse or misuse of hepatitis C treatments were considered very small
    - However, rebate agreements are such that if PA criteria are placed upon simeprevir and sofosbuvir, PA criteria must also be placed upon boceprevir and telaprevir.
        - Boceprevir 2011 and telaprevir 2011 are preferred on Utah Medicaid's Preferred Drug List.
        - Simeprevir 2014 and sofosbuvir 2014 have not been reviewed by the Pharmacy and Therapeutics Committee (do not appear on the Preferred Drug List)
- Based largely upon cost considerations, Utah Medicaid is considering prior authorization requirements for simeprevir 2014 and sofosbuvir 2014. Prior authorization criteria would serve to keep use on-label, particularly concerning viral genotype and subtype.
    - Possible prior authorization criteria is attached

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